REMARKS

Claims 1-18 are currently pending in the application. Claims 1-2, 4-8, and 10-12 are currently under consideration in the application, claims 3, 9, 13-18 having been withdrawn from consideration by a previous election/restriction requirement. The foregoing separate sheets marked as "Listing of Claims" shows all the claims in the application, with an indication of the current status of each.

35 U.S.C. §103(a) Rejection

Claims 1, 2, 4-8 and 10-12 stand rejected under 35 U.S.C. §103(a) as unpatentable over the Sensorcaine® with epinephrine (bupivacaine) entry of the PDR in view of the Corevert® (ibutilide) entry of the PDR. The Examiner states that the Sensorcaine® entry of the PDR teaches a composition employed in a method of inducing local anesthesia. Further, the Examiner states that the entry describes that epinephrine reduces the rate of absorption and peak plasma concentration of bupivacaine, permitting the use of moderately larger doses and sometimes prolonging the duration of the action. Examiner states that the PDR reference also teaches that bupivacaine is known to have adverse cardiovascular system reactions such a arrhythmia and even cardiac arrest. The Examiner further cites the Corevert® entry of the PDR as teaching the use of ibutilide as an antiarrhythmic drug. The Examiner then concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate ibutilide in a composition comprising bupivacaine and epinephrine, employed in a method of inducing analgesia. Examiner further states that one would have been motivated to do so because bupivacaine had been known to cause systemic cardiovascular effects, and ibutilide is an agent known for its antiarrhythmic properties. Thus, according to the Examiner, one would have been motivated to incorporate ibutilide into a regimen comprising bupicavacine and epinephrine in order to lower the incidence of bupivacaine adverse effects, thereby increasing the potency of bupivacaine.

Applicant respectfully disagrees with Examiner's analysis and conclusions. The PDR discussion of bupivacaine outlines several aspects of administration of the drug, with and without epinephrine, including an extensive review of potential deleterious side effects. Applicant concurs that prominent among those is the danger of arrhythmia, particularly when epinephrine is

included with the anesthetic, and especially when associated with unintentional intravascular injection. However, arrhythmia can also develop in any patient, particularly in the elderly, children, those with impaired heart, respiratory, or liver function, etc. The PDR reference teaches that bupivacaine should be administered only by qualified clinicians, and only with "Careful and constant monitoring of cardiovascular and respiratory vital signs..." (third page of Examiner's FAX of Dec. 18, 2003, middle column). However, there is absolutely no teaching or suggestion concerning the desirability of co-administering an antiarrythmic agent with a local anesthetic. The response of a patient to the drug is described in a manner that suggests that the response is highly individualized and unpredictable. In most cases of the use of this local anesthetic, no adverse side effects are observed. The PDR teaches that the administration of test doses are recommended (second column of third page of Examiner's FAX) along with "careful and constant monitoring" but there is no suggestion that prophylactic administration of an antiarrythmic agent would be advisable.

The PDR reference for ibutilide teaches that this agent may be used for the "rapid conversion of atrial fibrillation or atrial flutter of recent onset to sinus rhythm." (third column of second page of Examiner's FAX). There is no showing or suggestion that ibutilide could or should be used prophylactically or in combination with any other drug. Further, if arrhythmia developed, many agents are available for use by the clinician. Examiner states that it would be obvious to use ibutilide, but does not give any reason for that particular choice. In fact, it might not be the first choice of a physician since the PDR lists one potential side effect of ibulilide as inducing or worsening ventricular arrhythmia (third column of second page of Examinr's Dec. 18, 2003 FAX).

Applicant submits that the combination of bupivacaine plus ibutilide might be far worse for a patient than bupivacaine alone, or bupivacaine plus a different antiarrythmia agent since a patient that might otherwise be asymptomatic for arrhythmia due to bupivacaine, might develop arrhythmia due to ibutilde. Thus, to administer the two in combination prior to the development of arrhythmia symptoms under the assumption that potential arrhythmia would of a certainty be avoided, would be highly speculative, and would not be a reasonable "obvious" combination, as stated by Examiner.

Applicant further notes that a combination of bupivacaine and ibutilide, given the dose recommendations for each individually as taught in the PDR reference, would defeat the purpose of the present invention. The present invention provides a method of increasing the potency of an amide- or ester-linked local anesthetic by co-administering at least one methanesulfonamide compound. As a result of the increase in potency, a significantly lower dose of the local anesthetic can be used to obtain the same anesthetic effect. Further, the amount of methanesulfonamide compound that is used in the practice of the present invention is also much lower than that which would be used for the treatment of arrythmia. (See extensive discussion on page 18, lines 8-29 of the present application). Thus, both bupivacaine and ibutilide are used in the practice of the present invention at very low dosages, thereby decreasing the risk of toxicity and harmful side effects, but maintaining the same level of anesthetic capability. In fact, the doses that are used in the practice of the present invention would be ineffective to induce anesthesia (bupivacaine) or treat arrhythmia (ibutilide) if employed alone.

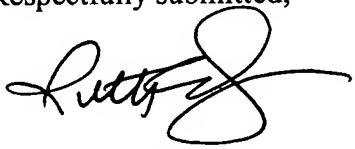
In summary, neither the PDR reference for bupivacaine or the PDR reference for ibutilide shows or suggests the use of the two in combination, and no "combination" of the teachings of the PDR references cited by Examiner result in the method of claims 1, 2, 4-8 and 10-12 of the present invention.

In view of the foregoing, it is requested that the application be reconsidered, that claims 1, 2, 4-8 and 10-12 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: clyde@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



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